64. (New) An aerosol spray which comprises an amount of descarboethoxyloratadine, or a pharmaceutically acceptable salt thereof, an amount of a decongestant, and a pharmaceutically acceptable carrier.

65. (New) An elixir which comprises an amount of descarboethoxyloratadine, or a pharmaceutically acceptable salt thereof, an amount of a decongestant, and a pharmaceutically acceptable carrier.

66. (New) A pharmaceutical composition which comprises from about 0.1 mg to 5 mg descarboethoxyloratadine, or a pharmaceutically acceptable salt thereof, a non-steroidal anti-inflammatory agent, and a pharmaceutically acceptable carrier.

67. (New) A pharmaceutical composition which comprises descarboethoxyloratadine, or a pharmaceutically acceptable salt thereof, a non-narcotic analgesic, and a pharmaceutically acceptable carrier.

68. (New) The pharmaceutical composition of claim 66 or 67 wherein the amount of descarboethoxyloratadine is from about 0.2 mg to about 1 mg.

REMARKS

Claims 48, 50, and 52-61, as amended, and new claims 63-68 appear in this application for the Examiner's review and consideration.

The title has been amended to more accurately reflect the pending claims.

Claims 49, 51 and 62 are canceled without prejudice herein. Claims 15-47 were canceled without prejudice in the Preliminary Amendment filed June 28, 1998. Applicants further note that claims 1-14 were canceled as indicated in the Patent Application Fee Sheet filed March 18, 1998.

New claims 63-68, which have been added herein, are supported by the specification and claims as originally filed. New claim 63 recites a pharmaceutical composition comprising from about 0.2 mg to about 1 mg of descarboethoxyloratadine ("DCL"), or a pharmaceutically acceptable salt thereof, an amount of a decongestant, and a pharmaceutically acceptable carrier. *See* Specification at page 14, line 17. New claim 64 recites an aerosol spray which comprises an amount of DCL, or a pharmaceutically

acceptable salt thereof, an amount of a decongestant, and a pharmaceutically acceptable carrier. *See* Specification at page 15, lines 12-17 and page 16, lines 22-29. New claim 65 recites an elixir which comprises an amount of DCL, or a pharmaceutically acceptable salt thereof, an amount of a decongestant, and a pharmaceutically acceptable carrier. *See* Specification at page 15, lines 12-17 and page 16, lines 22-29. New claim 66 recites a pharmaceutical composition which comprises descarboethoxyloratadine, or a pharmaceutically acceptable salt thereof, a non-steroidal anti-inflammatory agent, and a pharmaceutically acceptable carrier. *See* Specification at page 8, lines 18-25 and page 15, lines 12-17. New claim 67 recites a pharmaceutical composition which comprises descarboethoxyloratadine, or a pharmaceutically acceptable salt thereof, a non-narcotic analgesic, and a pharmaceutically acceptable carrier. *See* Specification at page 8, lines 32-37 and page 15, lines 18-25. New claim 68 recites an amount of descarboethoxyloratadine from about 0.1 mg to about 10 mg. *See* Specification at page 14, lines 11-15. Thus, no new matter has been added.

The Rejections Under §§ 101 and 112 Have Been Obviated

Claims 1-7 were rejected under 35 U.S.C. § 101 over U.S. Patent No. 5,595,997 for the reasons set forth on pages 2-3 of the Office Action. Further, claims 8-14 were rejected under 35 U.S.C. § 101 over U.S. Patent No. 5,731,319 for the reasons set forth on page 3 of the Office Action. As noted above, however, claims 1-14 were canceled at the time this application was filed. Applicants respectfully request acknowledgment of the cancellation of claims 1-14 and withdrawal of the rejection under U.S.C. § 101.

Claims 1, 8, and 48-62 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In particular, the Examiner alleges that the acronym "DCL" is noted but has not been accompanied by a common or more preferably an IUPAC chemical name. As suggested by the Examiner and for the sake of clarity, each of claims 50 and 54-59 have been amended to recite descarboethoxyloratadine. Further, claim 48 and 54-59 were amended to recite the features of claim 51 wherein the pharmaceutical composition further comprises a pharmaceutically acceptable carrier. *See, e.g.*, Specification at page 15, lines 12-17. For the above reasons, the rejections of claims 1-14 and 48-62 under 35 U.S.C. § 112, second paragraph, should be withdrawn.

The Rejections Under § 102 Have Been Obviated

Claims 48-54 and 60-62 were rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by U.S. Patent 4,659,716 to Villani *et al.* ("Villani") for the reasons set forth on pages 3-4 of the Office Action. Applicants respectfully traverse this rejection for the reasons provided below.

As the Examiner is aware, anticipation can only be established by a single prior art reference which discloses *each and every element* of the claimed invention. *Structural Rubber Prod. Co. v. Park Rubber Co.*, 221 U.S.P.Q. 1264 (Fed. Cir. 1984). Further, it is well established that a claimed range of values is not anticipated by a reference which discloses a range that touches, overlaps or is within the claimed range if the reference does not disclose specific examples falling within the claimed range. Indeed, the claimed range must be disclosed by a reference with "sufficient specificity to constitute an anticipation under the statute." Manual of Patent Examining Procedure, § 2131.03 (July 1998) (MPEP). "The question of 'sufficient specificity' is similar to that of 'clearly envisaging' a species from a generic teaching." *Id.* (citation omitted).

Villani discloses a general class of compounds, 7- and 8-(halo or trifluoromethyl)-substituted-6,11-dihydro-11-(4-piperidylidene)-5H-benzo[5,6]cyclohepta-[1,2-b]pyridines. Villani, col. 1, lines 17-38. But while Villani also suggests pharmaceutical compositions containing these compounds, it does not disclose even one pharmaceutical composition that contains a *specific* 7- or 8-(halo or trifluoromethyl)-substituted-6,11-dihydro-11-(4-piperidylidene)-5H-benzo[5,6]cyclohepta-[1,2-b]pyridine. *See, e.g.*, Villani, col. 1, lines 43-45; col. 8, lines 44-46. In particular, Villani does not disclose a pharmaceutical composition comprising the specific compound DCL and a decongestant, as claimed in claims 48 and 50-53. Villani merely mentions that pharmaceutical preparations can be made which comprise "from 1 mg to 1000 mg" of the "active compound" which can "also contain other therapeutic agents, such as decongestants." Villani, col. 8, lines 42-46.

As amended, claim 48 recites a pharmaceutical composition that comprises from about 0.1 mg to about 5 mg DCL and an amount of decongestant. Villani clearly does not anticipate this composition for at least two reasons. First, Villani fails to specifically disclose *any* pharmaceutical compositions comprising DCL, much less a pharmaceutical

composition comprising DCL and a decongestant.[1] Second, the amount of DCL recited by amended claim 48 is drastically less than that which is at best only suggested by Villani. Indeed, Villani suggests a maximum amount of an "active ingredient" which is *200 times* greater than that recited by amended claim 48. Further, only about the bottom 1% of the range suggested by Villani overlaps with that recited by amended claim 48. Consequently, Applicants respectfully submit that the claimed amount of DCL is not disclosed with sufficient specificity by Villani to read on an element of the claimed invention. For these reasons, Applicants respectfully request that the rejection of claims 48, 50, and 52-53 under § 102 be withdrawn.

The invention as recited by claims 54 and 60-61 is also not anticipated by Villani. Independent claim 54 recites a pharmaceutical composition that comprises DCL, or a pharmaceutical salt thereof, pseudoephedrine, and a pharmaceutically acceptable carrier. Villani, however, only suggests that pharmaceutical compositions can be formulated to contain a 7- or 8-(halo or trifluoromethyl)-substituted-6,11-dihydro-11-(4-piperidylidene)-5H-benzo[5,6]cyclohepta- [1,2-b]pyridine and another "therapeutic agent, such as decongestants." Villani, col. 8, lines 42-46. Villani does not disclose a specific pharmaceutical composition comprising DCL. Villani further does not disclose a single specific decongestant, much less pseudoephedrine.[2] Therefore, Villani cannot anticipate a pharmaceutical composition specifically containing DCL and pseudoephedrine.

Furthermore, the Examiner uses a combination of Villani and The Merck Manual, 16th Ed., Merck Research Laboratories, 326-332 and 2345-2346 (1992) ("Berkow") to anticipate claims 54 and 60-61. However, Applicants respectfully submit that such a combination is deemed improper under 35 U.S.C. §102(b) because the second reference is cited to fill in the limitation that is missing from an anticipatory reference. Legally, this is improper. "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. V. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir.

---

[1] For this reason alone, Applicants respectfully submit that the invention as recited by *original* (*i.e.*, unamended) claim 48 is not anticipated by Villani. Claim 48 has been amended, however, to further prosecution of this application.

[2] While it is made clear in the Office Action that Berkow is cited only to provide a definition of a specific compound allegedly known in the art to be a "decongestant," Applicants note that its disclosure of pseudoephedrine is irrelevant to the alleged anticipation of the invention by Villani, and that it is improper to combine references in order to allege anticipation under §102(b).

1987); see also *Atlas Powder Co. v. E.I. DuPont de Nemours & Co.*, 224 USPQ 409 (Fed. Cir. 1984) (the absence from a cited reference of any element of a claim negates anticipation of that claim by that reference). For these reasons, Applicants respectfully submit that the invention as recited by claim 54 is not anticipated by Villani. Applicants further submit that because the ranges of "active ingredient" disclosed by Villani do not even remotely disclose the amount of DCL recited by dependent claim 60, the rejection of claims 60-61 under § 102 should also be withdrawn.

The Rejections Under §103 Have Been Obviated

Claims 48-54 and 60-62 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Villani and Berkow for the reasons set forth on pages 4-5 of the Office Action. Applicants respectfully traverse this rejection.

As the Examiner is well aware, three basic criteria must be met to establish a case of *prima facie* obviousness: first, there must have been at the time of the invention a motivation to combine the references cited; second, the alleged prior art must teach or suggest all of the limitations of the claims alleged to be obvious; and third, there must have been at the time of the invention a reasonable expectation of success. MPEP § 2142. It is further well settled that the disclosure of a genus does not by itself render obvious a species within that genus, and that absent the further teaching or suggestion of a specific composition, the disclosure of a large genus of compounds does render obvious a specific composition comprising one of them. *See, e.g.*, MPEP § 2144.08; *In re Baird*, 29 USPQ2d 1550, 1552 (Fed. Cir. 1994); *In re Jones*, 21 U.S.P.Q.2d 1941, 1943 (Fed. Cir. 1992).

Villani discloses a class of compounds, 7- and 8-(halo or trifluoromethyl)-substituted-6,11-dihydro-11-(4-piperidylidene)-5H-benzo[5,6]cyclohepta-[1,2-b]pyridines. Villani, col. 1, lines 17-38. As is readily apparent to those skilled in the art, Villani discloses at least over 100 individual compounds. Villani further discloses a pharmaceutical composition comprising an *undisclosed species* of 7- and 8-(halo or trifluoromethyl)-substituted-6,11-dihydro-11-(4-piperidylidene)-5H-benzo[5,6]cyclohepta-[1,2-b]pyridines in an *unspecified amount* ranging from 1 mg to 1000 mg in optional combination with a second "therapeutic agent," such as a decongestant. Villani, col. 8, lines 42-47. As recognized by the Examiner on page 5 of the Office Action, Villani does not disclose a specific decongestant.

Berkow discloses an antihistamine-decongestant composition containing the decongestant pseudoephedrine. Berkow, page 326. As recognized by the Examiner on page 5 of the Office Action, Berkow does not disclose a specific antihistamine, much less a non-sedating antihistamine, such as DCL.

As amended, claim 48 recites a pharmaceutical composition that comprises from about 0.1 mg to about 5 mg DCL and an amount of decongestant. This composition is clearly not rendered obvious by Villani alone or in combination with Berkow for the following reasons. First, Villani provides no disclosure or suggestion of a pharmaceutical composition comprising the *specific* compound DCL, which is only one of the many species encompassed by the genus disclosed by Villani, and a decongestant. Indeed, Applicants respectfully submit that only with the aid of impermissible hindsight can the specific combination of DCL and a decongestant be identified from the broad disclosure that a 7- or 8-(halo or trifluoromethyl)-substituted-6,11-dihydro-11-(4-piperidylidene)-5H-benzo[5,6]cyclohepta-[1,2-b]pyridine can be combined with another "therapeutic agent." For this reason, Applicants further submit that even in combination with Berkow, Villani provides no suggestion of a pharmaceutical composition comprising DCL and pseudoephedrine, such as is recited by claim 54, much less the required expectation of success. This is because, assuming *arguendo* that there is motive to combine them, the combination of the two references suggests only that one of ordinary skill in the art try a pharmaceutical composition comprising pseudoephedrine and one of the over 100 compounds disclosed by Villani. As the Examiner is aware, "obvious to try" is not the proper standard. *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F2d 1367, 1380 (Fed. Cir. 1986). Therefore, the claimed invention is not rendered obvious.

The invention as now recited by claims 48, 50, 52-54, and 60-61 is further not obvious over Villani alone or in combination with Berkow because neither reference provides a suggestion of a pharmaceutical composition comprising the specific compound DCL in an amount of from about 0.1 mg to about 5 mg. Indeed, by suggesting a range of "active ingredient" of from 1 mg to 1000 mg (col. 8, lines 42-47), and by providing examples wherein the amount of the single active ingredient is either 100 mg or 500 mg (*see, e.g.*, col. 22, lines 39 and 63), Villani teaches away from the small amounts of DCL that are combined with another active ingredient as recited by claims 48 and 60. Consequently, at the time of this invention, one skilled in the art would have had no reasonable expectation that compositions comprising such small amounts of one specific compound within the large

genus disclosed by Villani would have any of the advantages disclosed by the present application. *See, e.g.*, Specification, page 5, lines 1-10.

In sum, neither Villani nor Berkow suggest, of the large number of compounds disclosed by Villani, DCL in an amount of from about 0.1 mg to about 5 mg and a decongestant, such as pseudoephedrine, much less provide the required reasonable expectation of successfully arriving at the claimed invention. Applicants thus respectfully request that the rejection of claims 48, 50, 52-54, and 60-61 under § 103 be withdrawn.

Claims 55-62 were rejected under 35 U.S.C. §103(a) as being unpatentable over Villani and Remington's Pharmaceutical Sciences, 18th Ed., Philadelphia College of Pharmacy and Science, 1097-1130 (1990) ("Gennaro") for the reasons set forth on pages 6-8 of the Office Action. Applicants respectfully traverse this rejection.

Villani discloses "other therapeutic agents" which encompass an undisclosed and a vast, if not infinite, number of compounds. However, Villani does not specifically disclose non-steroidal anti-inflammatory agents or non-steroidal analgesics, much less disclose an example of either.

Genarro discloses pharmaceutical compositions containing antihistamines and mild analgesics. However, Genarro fails to specifically disclose DCL. Genarro also fails to specifically disclose combinations of DCL and a non-steroidal anti-inflammatory agent or non-narcotic analgesic.

Claims 55-61 recite pharmaceutical compositions comprising DCL and a specific non-steroidal anti-inflammatory agent or non-narcotic analgesic. This composition is clearly not rendered obvious by Villani alone or in combination with Genarro for the following reasons. Villani provides no disclosure or suggestion of a pharmaceutical composition comprising the *specific* compound DCL, which is only one of the many species encompassed by the genus disclosed by Villani, and a non-steroidal anti-inflammatory agent or non-narcotic analgesic. Further, when combined with the at least one hundred 7- or 8-(halo or trifluoromethyl)-substituted-6,11-dihydro-11-(4-piperidylidene)-5H-benzo[5,6]cyclohepta-[1,2-b]pyridines disclosed by Villani, the vast, if not infinite, number of "other therapeutic agents" does not even remotely suggest the specific combination of DCL and a non-steroidal anti-inflammatory agent or non-narcotic analgesic, as claimed herein. Indeed, Applicants respectfully submit that only with the aid of impermissible hindsight can the specific combination of DCL and a non-steroidal anti-inflammatory agent or non-narcotic analgesic be identified from the broad disclosure that a 7- or 8-(halo or

trifluoromethyl)-substituted-6,11-dihydro-11-(4-piperidylidene)-5H-benzo[5,6]cyclohepta-[1,2-b]pyridine can be combined with another "therapeutic agent." For this reason, Applicants further submit that even in combination with Genarro, Villani provides no suggestion of a pharmaceutical composition comprising DCL and a non-steroidal anti-inflammatory agent or non-narcotic analgesic, as recited by claims 66-68, much less a pharmaceutical composition comprising DCL and the specific non-steroidal anti-inflammatory agents or non-narcotic analgesics recited by claims 55-61. This is because, assuming *arguendo* that there is a motive to combine, the combination of the two references suggests only that one of ordinary skill in the art try a pharmaceutical composition comprising a mild analgesic and one of the vast number of compounds disclosed by Villani. At best, Villani and Genarro render the combination of DCL and a non-steroidal anti-inflammatory "obvious to try." This is not, however, the proper test of obviousness. *Hybritech*, 802 F2d at 1380. Thus, the combination of Villani and Genarro does not suggest the claimed invention, much less provide a reasonable expectation of success. Further, the combination of Villani and Genarro requires one of ordinary skill in the art to impermissibly "pick and choose" DCL of Villani and an analgesic of Genarro, which is only possible when using the present claims as a blueprint, which is improper. Thus, the combination of Villani and Genarro cannot obviate the present claims. For all the above reasons, Applicants respectfully request that the rejection of claims 55-61 under U.S.C. § 103(a) be withdrawn.

Conclusion

Applicants respectfully request the entry of the foregoing amendments and remarks into the file of the above-identified application. Applicants believe that all pending claims are now in condition for allowance, early notice of which would be appreciated. Should the Examiner deem it helpful, a personal or telephone interview is respectfully requested to discuss any remaining issues in an effort to expeditiously advance the application to allowance.

A fee of $390.00 is believed to be due for the claim changes of this response. A fee sheet, with provision for the required fee, is submitted herewith.

Respectfully submitted,

Date: July 11, 2000

Max Bachrach 45,479

Max Bachrach (Reg. No.)

For: Stanton T. Lawrence, III (Reg. No. 25,763)

PENNIE & EDMONDS LLP
1667 K Street N.W., Suite 1000
Washington D.C. 20006

(202) 496-4400

Enclosures